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IN THE GUINEA-PIG.

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(*From the Sears Pathological Laboratory, Harvard Medical School.*)

PLATES XIX AND XX.

I. A CASE OF HUMAN GLANDERS.

ON account of the rarity of glanders infection in man in this country, and in view of the apparent uncertainty which exists regarding the histology of the lesions of the disease, the following case is of interest:

Clinical History.—The patient, an adult male, entered the Malden (Massachusetts) Hospital October 24, 1895, in the service of Dr. J. Richmond Barss, with a gangrenous condition of the middle finger and extensive suppuration in the hand. His history, which was obtained later, was as follows: On September 30th, while skinning a farcy horse, he cut his finger. The next day his finger pained him, but did not appear to be injured. The pain continued, and he took to his bed, where he was seen by a physician eight days later, who diagnosed a felon and incised the finger. He remained in bed with fever and great thirst until October 24th, when he was admitted to the hospital. His temperature some hours after entrance was 105° F. The next day amputation of the finger at the metacarpo-phalangeal articulation was performed.

About the fourth day after admission pustules appeared on the forehead and upon other parts of the body. Later those on the forehead became

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confluent and underwent ulceration, while symptoms of marked septic poisoning developed, the temperature reaching 105° F. There were no nasal symptoms. Death occurred November 1st, one week after entrance into the hospital and thirty-one days after receiving the wound in the finger.

Autopsy.—Five hours after death. The body is that of a well-built, muscular man. Subcutaneous fat moderate in amount. Rigor mortis very marked. Slight lividity of dependent portions. Amputation of finger.

The skin of the forehead as low as the eyebrows and of the scalp as far back as the vertex is thickened, discoloured, eroded, and feels dense to the touch. The margin of this area is escalloped, and is rather sharply elevated above the adjoining normal skin. In colour it is purple, mottled with small yellow areas. Over the upper portion of the forehead and at the beginning of the scalp the epidermis is purple to black in colour, and more or less detached from the underlying tissue, from which it can be easily removed. In places it is lacking, leaving irregular and rather superficial ulcerations, in which there can be made out many yellow specks, not soft enough to be called pus. On section the tissue is deeply infiltrated with an opaque, yellowish-white material, which is rather firm, and can not be squeezed out like pus. In the left upper eyelid are several pustules, single and grouped. Over the zygomatic arch and on the right side there are also two small groups of pustules. In the skin of the left arm, on its outer and posterior surfaces, are scattered several pustules from one to three millimetres in diameter and about one millimetre in elevation. Three or four similar pustules are seen on the skin of the right arm, and one on the skin over the tibia. On the front of the chest are two pustules, besides a small group below the outer end of the left clavicle. The pustules found in these situations generally present a purplish tint about their bases. In the pectoral muscle on the right side, near the sterno-clavicular articulation, is a small, oval, yellow, semi-solid nodule about the size of a split pea. The left axilla contains an area of suppuration in the axillary fatty tissue about 5 centimetres long and 3 centimetres in diameter. On section, this area resembles a bit of very coarse sponge, the meshes of which are filled with a thin, odourless, yellowish fluid. Some of the lymphatic glands in the neighbourhood are still well preserved, although considerably enlarged, and on section they show a yellow infiltration on the side toward the pus.

Lungs.—The left lung over the upper lobe is bound down by fibrous adhesions. The right lung is free. Both are moderately congested, and slightly oedematous posteriorly. On the lower surface of the right upper

lobe are two yellow, elevated areas, 2 millimetres in diameter, surrounded by a dark-red zone. The pleura over both areas is covered with a thin coat of fibrin. Scattered through the remainder of the right lung, usually just beneath the pleura, are in all about a dozen small resistant areas, the largest not more than 1 centimetre in diameter. On section, these areas are sometimes found to be solid, of a dark-red colour, with yellow points; sometimes softened or broken down, forming abscesses or cavities filled with fluid of a purulent character. On the pleura over these areas there is often a thin fibrinous exudate.

Heart.—Not remarkable.

Spleen.—Enlarged to half again its normal size; soft. Follicles not visible on section.

Kidneys.—Capsule very slightly adherent. On section, cortex more opaque than normal. Pyramids injected.

Liver.—Slight cloudy swelling.

The deep cervical and mesenteric lymphatic glands slightly enlarged and congested.

The nasal cavities and pharynx were not examined.

BACTERIOLOGICAL EXAMINATION.—Cover-glass preparations from the lesions on the scalp and from the pus of the axillary abscess showed the presence of a few bacilli of medium size, with rounded ends, varying in length, and having faintly staining spaces in the protoplasm. The purulent-looking fluid from a small abscess cavity in the lung was negative on cover-glass examination. Cultures were made on coagulated blood serum (Löffler's mixture) in test tubes from the various lesions and from the organs, with the following results, after about thirty-six hours in the incubator:

Pus from the Axillary Abscess.—The surface of the culture medium was thickly sown with discrete and confluent colourless colonies, resembling small drops of dew, and varying in diameter from a pin point to about 1.5 millimetre. The growth was slow, the colonies being barely visible after twenty-four hours.

Cutaneous Lesions.—Cultures were made from four different places, including the ulcerated tissue of the scalp and the pustules, with the following results:

Culture No. 1: Very numerous yellow colonies and a few minute colourless colonies. The former were colonies of the *staphylococcus pyogenes aureus*.

Culture No. 2: A few small colourless colonies and numerous colonies of the staphylococcus pyogenes aureus.

Culture No. 3: Very numerous discrete and confluent colourless, wet-looking colonies, of the same appearance as those in the culture from the axillary abscess.

Culture No. 4: Rather numerous colourless, moist-looking colonies, the largest about 1 millimetre in diameter. A very few contaminating colonies present.

Abscess of Lung.—Only three or four colonies developed. These were small, colourless and moist-looking, the largest about 1 millimetre in diameter.

Spleen.—Half a dozen of the same colourless, moist-looking colonies.

Kidney.—One colony of an unknown organism.

Liver.—Some unknown bacteria.

Blood of the Heart.—Sterile.

The colourless colonies which were present in the cultures from the pus of the axillary abscess, cutaneous lesions, abscess of the lung, and the spleen, were found to be composed of one and the same organism—namely, a bacillus of medium size, with rounded ends and of variable length. It was usually short, but sometimes appeared in long forms, which were slightly wavy or curved. Its protoplasm frequently showed irregularly distributed, faintly staining areas. The shorter forms occurred frequently in pairs, and showed an ill-defined faintly stained space in the centre of the rod. The colonies on blood serum, if well separated, attained after a time a diameter of several millimetres. At first they were colourless, translucent, and viscid-looking, but later they assumed a brown tint. Pure cultures were obtained on potatoes of the bacilli from all of the original cultures. The appearances of all these potato cultures were the same. After thirty-six hours in the incubator the growth appeared in the form of a moist, translucent, viscid-looking material. Later this acquired a brown colour, and resembled honey in appearance. After a few days it became a darker brown, lost its translucency, and the potato around took on a dark-gray colour. The growth of the bacilli in cultures was slow, thirty-six hours being required for a fair development.

The morphological and cultural peculiarities above described are identical with those of the bacillus of glanders.

RESULTS OF THE INOCULATION OF GUINEA-PIGS.—Guinea-pigs were inoculated with young blood-serum cultures of the bacilli derived from each of the original cultures. In inoculating, either a suspension in sterilized salt solution was injected with a hypodermic syringe or the material from the cultures was introduced beneath the skin through a wound by means of a platinum wire. The quantity of the suspension injected was not more than about 0.5 cubic centimetre for each animal, except in the case of one which received 1 cubic centimetre. The chief results of these inoculations were as follows:

BACILLI FROM THE AXILLARY ABSCESS.

Guinea-pig No. 1: Subcutaneous inoculation in abdominal wall. Death after twenty-one days. Ulcer at point of inoculation; abscess of scrotum; abscess of inguinal lymphatic gland; abscess of anterior nares; small nodules in spleen and liver.

Guinea-pig No. 2: Inoculation into peritoneal cavity. Death in forty-eight hours. Nodules in testicular membrane; fibrinous peritonitis, with minute grayish granulations; adrenal glands and lymphatic glands haemorrhagic.

BACILLI FROM CUTANEOUS LESIONS.

Culture No. 1: Subcutaneous inoculation in abdominal wall. Death after twenty-four days. Ulcer at point of inoculation; ulcer of scrotum; abscess of testicle; abscess of inguinal lymphatic gland; nodules in spleen and liver.

Culture No. 2: Subcutaneous inoculation in left thigh. Ulcer at point of inoculation. Killed after eight days. No characteristic lesions.

Culture No. 3; Guinea-pig No. 1: Subcutaneous inoculation in abdominal wall. Killed after sixteen days. Ulcer at point of inoculation; yellow nodules beneath membranes of testicles; abscess of dorsum involving vertebrae.

Guinea-pig No. 2: Subcutaneous inoculation both in abdominal wall and in thorax. Death after fourteen days. Ulcer at point of inoculation; nodules in testicle and in spleen.

Culture No. 4: Inoculation in peritoneal cavity. Death in four days and a half. Oedema and congestion of scrotum; purulent infiltration of membranes of testicle; localized fibrinous peritonitis; nodules in spleen.

BACILLI FROM THE ABSCESS OF LUNG.

Guinea-pig No. 1: Inoculation into peritoneal cavity. Death in thirty-six hours. Small nodules in omentum, liver, and spleen; lymphatic glands haemorrhagic.

Guinea-pig No. 2: Death after twenty-two days. Abscess of testicle; abscess of anterior nares; suppuration about joints involving the bone; abscess of inguinal lymphatic glands; nodules in liver; large nodule in spleen.

BACILLI FROM THE SPLEEN.

Guinea-pig No. 1: Inoculation in the peritoneal cavity. Death in thirty-six hours. Small nodules in peritonæum, spleen and liver; omentum infiltrated with fibrino-purulent exudation; lymphatic glands haemorrhagic.

Guinea-pig No. 2: Subcutaneous inoculation in abdominal wall. Culture derived from the spleen of guinea-pig No. 1. Death after twelve days. Ulcer at point of inoculation; ulcer of scrotum; adhesive inflammation of membranes of testicles, with formation of yellow foci.

Summing up the results of the animal inoculations, it may be said that the bacilli found in at least six of the seven original cultures produced the characteristic lesions of experimental glanders in the guinea-pig—namely, the acute inflammatory lesions of the scrotum or testicle and the grayish, tuberclelike nodules in various situations. The negative result in the case of the bacilli from one of the original cultures may be explained by the fact that the animal was killed before sufficient time had elapsed for metastases to take place, the bacilli at the time of the killing of the animal being still localized at the point of inoculation. The organism inoculated into the animal was identical in morphology and cultural peculiarities with those of the other cultures. The bacteriological examination of the case, therefore, showed the presence of a bacillus in the axillary abscess, in the lesions of the skin and lungs, and in the spleen, which, on account of its morphology, mode of growth upon potatoes and pathogenic effects on guinea-pigs, must be considered to be the bacillus of glanders.

Two guinea-pigs were also inoculated respectively with the pus of the axillary abscess and with the purulent fluid from a small ab-

scess or broken-down nodule in the lung, from which a few colonies of glanders bacilli were cultivated. The inoculations were made into the peritoneal cavity by incision. The animal inoculated with the pus of the axillary abscess showed swelling of the scrotum, and was killed after seventy-two hours. At autopsy, yellowish nodules were found in the testicles and a few similar nodules in the peritonæum. The animal inoculated with the purulent fluid from the lung nodule was killed after fifteen days. The scrotum was markedly swollen and the animal emaciated. The testicles contained caseous areas, and the membranes were infiltrated with inflammatory exudation, which also involved the scrotal tissues.

A number of cultures made from the inoculated animals resulted as follows: The bacillus was found in the liver in nine out of thirteen animals; in the spleen in eleven out of thirteen; in the kidney in two out of eleven; and in the blood of the heart in three out of eleven. The bacilli in the blood of the heart were few, and the cases in which they were found in that situation were rapidly fatal. In the kidney the bacilli were also present in but small numbers, whereas they were sometimes numerous in the spleen and liver.

A number of the lesions in the testicle and many of the areas of abscess formation in the lymphatic glands and elsewhere contained the bacilli in large numbers in apparently pure culture except in one instance.

HISTOLOGICAL EXAMINATION.—Sections were prepared from the lesions of the skin, the axillary abscess, lymphatic glands, lesions of the lungs, nodule in pectoral muscle, and from the kidney, spleen, and liver. For hardening, Zenker's fluid or alcohol, or both, were employed.

The stains used were haematoxylin with eosin, and fuchsin with aurantia. No satisfactory method of staining the bacilli in sections was found. The results of the study of these sections were as follows:

Lesions of the Scalp.—Under the low power the subcutaneous tissue seems to be more or less densely infiltrated with a purulent-looking material, containing very numerous small, deeply staining granules. In places some of the structure of the tissue is preserved;

in other areas no vestige of the original tissue remains, but foci are present which are made up of the above-mentioned material. Large lymph vessels near the muscular layer are seen filled with the same substances. The tissue immediately beneath the epidermis contains a large amount of blood. The epidermis in places is more or less disintegrated, the upper layer being separated from the lower layers by loose cells and detritus. The tissue beneath the muscle contains a large amount of fibrin and rather numerous nuclei.

Under the high power the infiltrating material resolves itself into polynuclear leucocytes, deeply stained chromatin fragments of varying size and shape, faintly stained nuclei, red blood-corpuscles, the empty membranes of dead cells or the skeletons of nuclei, together with necrotic detritus. The leucocytes and chromatin fragments in varying proportions constitute the greater part of the mass. The chromatin fragments vary in form and size from small granules to oval and irregular masses of the size of large cells. In the tissue beneath the muscular layer the nuclei observed with the low power are seen to belong to polynuclear leucocytes and to cells which belong to apparently proliferated lymphatic endothelium. The latter cells have oval vesicular nuclei and considerable cytoplasm. Polynuclear leucocytes are also seen in places between the fibres of the muscular layer.

In the disintegrated portions of the epidermis are seen many epithelial cells in all stages of disintegration, some polynuclear leucocytes and a few red blood-corpuscles, besides rather numerous delicate unstained ringlike bodies. These last vary in size from something less than that of a red blood-corpuscle to that of a polynuclear leucocyte, or are even larger. Some of them have a contracted and irregular shape, suggesting the membranes of dead cells. The origin of these bodies is not clear. Some of them apparently represent degenerated red blood-corpuscles.

A large pustule on the face presented essentially the same conditions as were observed in the more diffuse lesions of the scalp.

In a section through a small pustule 3 or 4 millimetres in diameter the corium and the epidermis, except the horny layer, have disappeared, and in the place of these are seen polynuclear leucocytes and

cellular detritus, besides a few red blood-corpuses and chromatin bodies. The neighbouring tissue for some distance is infiltrated with the same material. The pea-sized nodule in the pectoral muscle on section appeared under the low power as a necrotic-looking material. Under the high power this was seen to contain many leucocytes, frequently showing degenerative appearances and much cellular detritus. Masses of a reticulated substance resembling fibrin were also present, as well as many deeply staining granules and globules of chromatin.

Pulmonary Lesions.—A number of these were studied in sections. The sections of nodules or consolidated areas showed the alveoli in the peripheral portions to be filled with a material consisting of leucocytes, red blood-corpuses, and fibrin, together with proliferated alveolar epithelium. These elements were present in varying proportions in different places and in different sections. In some parts of the consolidated areas—particularly in the central portions—the walls of the alveoli have more or less disappeared, and have been replaced by a necrotic-looking material, containing numerous polynuclear leucocytes and some chromatin fragments. Small bronchi, devoid of epithelium, may be seen filled with this material. Sections of consolidated areas which have undergone extensive softening, and in some places are broken down, and of cavities containing fluid and detritus, were also studied. The softened material and the remains of the contents of the cavities were found to consist essentially of necrotic and degenerated cells, together with leucocytes in larger or smaller numbers. In one instance there was granulation tissue in the wall of the cavity. The histogenesis of the lesions in the lung seems to be the filling up of the alveoli with inflammatory exudation and proliferated epithelial cells followed by degeneration and necrosis in the area of consolidation so formed, resulting eventually in cavity formation. The process is essentially a focal pneumonia, with suppuration and necrosis.

Axillary Abscess.—The tissue involved showed an infiltration with large oval cells with vesicular nuclei, which were apparently derived from the lymphatic endothelium. These cells were often more or less degenerated, and in places formed nothing more than ne-

crotic detritus containing leucocytes. The necrotic material seems to represent the pus of the abscess.

Lymphatic Glands.—In the lymphatic glands in the neighbourhood of the axillary abscess it was possible to demonstrate proliferation of the endothelium of the lymph sinuses and coarse strands of fibrin in the blood vessels. Sections of other lymphatic glands presented no remarkable lesion.

The Kidneys.—Sections hardened in Zenker's fluid, and stained with fuchsin and aurantia, gave the following results: The epithelial cells of the cortical tubules are very granular, often separated from one another and projecting far into the lumen of the tubule. Many nuclei are stained more deeply and homogeneously than normal; others stain only faintly, and are more or less shrunken. In the lumina of most of the tubules a peculiar material is seen. This usually appears in the form of delicate rings or circles closely packed together, along with which are red-stained granules resembling chromatin. These rings vary in diameter from about that of a red blood-corpusele to that of a large nucleus of the renal epithelium. They are often distorted or irregular in outline. In some tubules the material has the appearance of an indefinite granular detritus staining more or less red. Material similar to that in the tubules is also to be seen in small amounts in the capsular spaces of the glomeruli. Its origin is obscure. Some of it may represent degenerated red blood-globules, but the study of the sections gave little evidence that such was the case. That it is the remains of degenerated and extruded nuclei is also suggested, but there does not seem to be a sufficient diminution in the number of nuclei in the renal epithelium to account for the great amount of it which is demonstrable. It is apparently the same as that seen in the renal tubules of the guinea-pig, as shown in Plate XX, Fig. 4.

The spleen showed the presence of a large amount of blood in the sections. *The liver* was not remarkable.

II. THE HISTOLOGICAL LESIONS OF EXPERIMENTAL GLANDERS IN THE GUINEA-PIG.

At the present time the generally accepted ideas of the histology of the glanders tubercle and of the histogenesis of its formation are those which were advanced by Baumgarten. This investigator states in his well-known "Lehrbuch der pathologischen Mykologie" that the histological composition of the experimental glanders tubercle and that of the miliary tubercle are essentially the same. He holds that the glanders tubercle, like the miliary tubercle, at first consists of epithelioid cells, among which leucocytes later appear, but that the two lesions differ mainly in the fact that the glanders tubercle undergoes necrotic and suppurative changes more quickly than the miliary tubercle. The epithelioid cells are, according to his observations, derived from the fixed tissue cells. According to Baumgarten, therefore, the primary effect of the bacillus of glanders upon a tissue is a new growth of cells with secondary degenerative changes rather than necrosis and suppuration from the beginning.

The evidence which Baumgarten offers in support of his views is not convincing. He states that he has seen epithelioid cells in glanders tubercles in mice and guinea-pigs; but his drawing of a section of a small glanders focus in the liver of a mouse would seem to show that what he considered to be epithelioid cells were none other than degenerated liver cells.

Since Baumgarten, Tedeschi* is apparently the only writer who has investigated the histology of the lesions of experimental glanders. He says that his observations have not enabled him to confirm the opinions of Baumgarten, but rather support the view that the primary effect of the bacillus of glanders upon a tissue is necrosis and the invasion of leucocytes. The difference between his results and those of Baumgarten, he suggests, may be due to the greater virulence of his cultures. Tedeschi's descriptions, however, of the histology of the lesions encountered in various situations are not very definite or altogether satisfactory.

* Ziegler's *Beiträge z. path. Anat.*, Bd. xiii, 1893.

From what has been said it is evident that the histology and histogenesis of the experimental glanders tubercle are still not clearly understood, and it is as a contribution to this subject that the following observations are offered:

Methods.—For the study of the histology of the lesions of experimental glanders paraffin sections of the tissues of nine of the inoculated guinea-pigs were prepared. Most of these tissues were hardened in both Zenker's fluid and in alcohol. The duration of the infection in the nine animals was thirty-six hours in the case of two, and forty-eight hours, four days and a half, fourteen, sixteen, twenty-one, twenty-two, and twenty-four days respectively in the remaining seven animals. The material for the study comprised sections of the livers, spleens, lungs, adrenals, and lymphatic glands of the nine guinea-pigs, of the kidneys of eight, of the testicles of seven, and of the peritoneal exudates from three.

The most satisfactory method of staining sections of tissue hardened in Zenker's fluid was found to be double staining with fuchsin and aurantia. The fuchsin was used in a solution made up of about 10 cubic centimetres of the saturated alcoholic solution with 100 cubic centimetres of water. Of aurantia an aqueous solution something below one per cent was employed. The demonstration of the bacilli in sections was found to be very difficult. Unless they were numerous, they could rarely be found. No satisfactory method for the staining of the bacilli in sections was arrived at, although many experiments with various methods were made with this end in view.

Liver.—This organ frequently presented minute grayish points and sometimes yellow areas. In the sections examined these yellow areas seemed to correspond to areas of necrosis of liver tissue, and the smaller grayish points to small glanders tubercles or foci. Under the low power the glanders tubercles appeared as foci or aggregations of small bodies of varying size and shape, staining deeply with fuchsin, and resembling at first sight collections of leucocytes. These foci were observed in the sections of eight out of the nine livers, usually in small numbers. Their size varied from about that of the area occupied by half a dozen liver cells upward. Under a high power they

were seen to consist of bodies staining deeply with fuchsin, polynuclear leucocytes, structures looking like the skeletons of dead nuclei of various kinds, and an indefinite material, apparently the remains of dead cells. A small glanders tubercle under a high power is shown in Plate XIX, Fig. 1. The deeply staining bodies were the most striking objects in the areas, and from their appearance they were evidently of the nature of chromatin. In shape and size they were very variable. Some were round, and ranged in size from that of a minute globule to that of a red blood-corpusele. Some were large, elongated, club-shaped, or constricted at the middle. Others were irregular or lobulated, as if from the fusion of several of the round forms. All were homogeneous and stained deeply. The smallest foci consisted essentially of broken-down liver cells, polynuclear leucocytes, tissue detritus, and a few of the chromatin fragments.

From a study of these areas in the liver it seems that the process of their formation consists in the degeneration and destruction of liver tissue and the invasion of polynuclear leucocytes, together with changes in the nuclei of the tissue cells and of the leucocytes, whereby the chromatin bodies are produced. There was no evidence of the production of the epithelioid cells of Baumgarten's description.

In addition to these lesions, other changes in the liver were met with. Among the more prominent was the occurrence of liver cells, isolated or in groups, whose nuclei were stained much more deeply and homogenously than usual (Plate XIX, Fig. 1), while the cytoplasm in some cases was also denser and more deeply stained. This deep staining of the nuclei was also seen in the areas of necrosis mentioned above, and in some instances about the glanders foci. In the bile ducts in some cases a granular material could be seen which, on close examination under a high power, was seen to consist mainly of delicate rings of about the diameter of the nuclei of the epithelial cells of the duct. Adherent to these rings or among them were minute fuchsin-stained granules. Similar indefinite, irregular rings, with red-stained granules, were also seen in some instances in the capillaries and lymph spaces. These, as well as the material in the bile ducts, suggested degenerated nuclei.

Spleen.—The presence of minute grayish nodules in the spleen in experimental glanders is very characteristic of the disease. In the sections from eight spleens small glanders foci were present in varying numbers. They did not occupy any special situation in the organ. Under the low power these foci appeared as aggregations of small deeply stained granules. Under the high power essentially the same elements were seen as in the foci in the liver. Chromatin bodies, of varying size and shapes, polynuclear leucocytes, faded-out nuclei, and cellular detritus were recognised in the material of which the area was composed. In some cases fibrin was also present. Sometimes the nuclei of the tissue immediately surrounding a focus stain faintly, as if undergoing degeneration. The smallest areas show the deeply staining bodies and a few leucocytes, together with a fading out or disappearance of the nuclei and a breaking up of the cytoplasm of the cells. As in the liver, the process seems to be one of necrosis and invasion by leucocytes, accompanied by certain degenerative changes in the nuclei, in consequence of which the chromatin bodies are formed.

In some cases masses of fibrin could be demonstrated in the sinuses by means of Weigert's fibrin stain.

Lungs.—In the sections from seven animals more or less well-developed glanders foci were found. These consisted essentially of the same material as was found in the foci in the livers and spleens—namely, numerous deeply red-staining bodies of variable size and shape, leucocytes, and cellular detritus. Unstained or faintly stained bodies, looking like faded and distorted nuclei of tissue cells and leucocytes, together with irregular ringlike structures resembling the empty membranes of dead cells, were also seen. In some instances the walls of the air cells were preserved to some extent; in others, they were not to be made out. From a study of the smaller, or what were considered as beginning foci, it would seem that these focal lesions are due to a proliferation of the epithelium of the air cells and the invasion of leucocytes, together with degenerative processes in these elements by which the chromatin bodies are formed.

In the bronchi a peculiar material was frequently present in large

amounts. This consisted mainly of delicate rings or circles, sometimes irregular, and varying in diameter, the largest being about the size of the nucleus of a bronchial epithelial cell. Minute fuchsin-staining granules were adherent to and also scattered among these rings. This material was similar to that observed in the bile ducts of the liver. The appearances of these rings suggested that they represented dead and extruded nuclei from the epithelium of the bronchus, but the absence of any marked diminution in the numbers of these nuclei seemed to negative this idea. That some of them at least may be degenerated red blood-corpuses seems possible.

Lymphatic Glands.—The lymphatic glands, especially in the rapidly fatal cases, were often enlarged and red. In the more chronic cases they were usually enlarged, and sometimes showed caseous areas or abscess formation. Sections of lymphatic glands from nine animals were studied. In two of these, four animals dying within forty-eight hours, nothing more than congestion and haemorrhage was made out. In the sections from seven animals, however, glanders lesions of varying size were seen. The larger foci, under a lower power, showed very numerous red-staining granules and fragments in an indefinite ground substance. Under a high power, in these foci were seen in great numbers the deeply red-stained bodies, of variable size and shape, which were observed in the lesions in other organs. Poly-nuclear leucocytes, structures which resembled the skeletons of nuclei and of cells, and an indefinite stroma of more or less fibrillar appearance made up the remainder of the material filling up the area. The presence of fibrin could not be demonstrated. What were considered to be beginning glanders foci were seen in the lymph follicles. These appeared as small areas in the follicles, where the nuclei were faintly stained, and in which a few deeply staining globules of varying size could be seen. In what was apparently a somewhat later stage, many of the cells of the follicles in such an area seemed to have broken up and the deeply stained globules were more numerous, while here and there a faded-out nucleus was observed. Some of the deeply stained bodies seemed to arise from changes in the nuclei of the tissue cells, for around some of them a certain amount of cytoplasm could be

seen. Sections hardened in Flemming's solution showed no evidence of fat in the foci. The process of formation of the glanders lesions in the lymphatic glands is apparently one of degeneration and necrosis with the later invasion of leucocytes, and is practically the same as occurs in other organs. The lesions do not seem to be the result of a primary proliferation of tissue cells, but are necrotic from the beginning.

Adrenals.—A more or less marked haemorrhagic condition was frequently observed in these organs. In three of the nine adrenal glands examined microscopically small irregular areas were observed in which the essential condition seemed to be the degeneration of the cells of the organ, with a subsequent invasion by polynuclear leucocytes. In these areas the same deeply stained granules and bodies of various shapes were again present, in addition to the polynuclear leucocytes. A deeper staining of the nuclei and cytoplasm of the large cells of the organ was also observed in some instances. This was apparently the same change as that met with in the liver cells.

Peritonæum.—After intraperitoneal inoculation, the peritonæum, both visceal and parietal, may present a fibrinous exudation with minute nodules or granulations, while the omentum may be shrivelled up and infiltrated with exudation. Sections were obtained through such granulations or nodules, as well as from the infiltrated omentum. Under a low power (Plate XX, Fig. 2) the granulations appear as rounded or oval aggregations of deeply stained granules in the midst of an indefinite material, the whole being held together and limited by fibrin. Under a high power the material making up the greater part of the nodule is seen to be of two kinds—viz., the same deeply red-stained granules and irregular bodies present in the lesions elsewhere and ringlike structures not stained red. The latter are usually round, but are often oval or irregular. They vary in diameter from that of a minute globule of chromatin to that of a large cell. These structures are very numerous, and seem to represent faded nuclei of polynuclear leucocytes and other cells, as well as the cell membranes of dead cells. They were observed in the lesions elsewhere, but in smaller numbers. The fibrin is disposed mostly about the periphery

and over the surface of the peritonæum in a more or less definite layer, little or none being found in the interior of the nodule. Nuclei of polynuclear leucocytes were only rarely made out in the peritoneal nodules. The omentum on section shows larger and smaller foci and fibrinous exudation. The material forming the foci was the same as that in the nodules in the peritonæum elsewhere.

Testicles.—The lesions in the testicles were of the same character as those observed in other situations. The process seemed to begin usually in the tunica vaginalis with the formation of nodules of the same kind as those observed on the peritonæum. The elements making up these nodules are shown in Plate XX, Fig. 3. From the tunica the process may extend to the testicle or toward the skin of the scrotum, and large areas may be formed made up of the same material as that found in the foci elsewhere. The lesions are here again distinctly suppurative from the beginning.

Kidneys.—In the sections of the kidney from eight of the inoculated guinea-pigs no glanders foci were seen. These organs, however, in some cases presented marked cloudy swelling and hyaline degeneration of the epithelium of the tubules. In addition to these lesions of the epithelium, a peculiar material was frequently seen filling the lumina of the tubules, and could also be demonstrated in the capsular space of the glomeruli, apparently the same as that seen in similar situations in the human kidney. This material in some places was of a granular character, with a tendency to stain red with fuchsin; in other places it was in the form of faintly red-staining rings, with red-stained adherent granules (Plate XX, Fig. 4). The rings were of variable size, the largest being somewhat larger than the nucleus of a renal cell. They were frequently distorted or irregular in outline. The nuclei of the epithelium of the tubules were often faded and shrunken. Some were deeply and homogeneously stained, presenting the same appearance as those described in certain of the liver cells.

The origin and nature of this material in the tubules and glandular spaces is not clear. Its general appearance would suggest that it is made up of degenerated and extruded nuclei of the renal epithelium, but there does not seem to be sufficient diminution in the num-

ber of these nuclei to give support to this idea. That it represents degenerated or altered red blood-corpuses does not seem probable, for the preparations hardened in Zenker's fluid, which is a good preservative for blood, showed no convincing evidence of such an origin.

CONCLUSIONS.

The glanders nodule in the class of cases studied by us is in no sense analogous to the miliary tubercle in its histogenesis, and our studies afford no support to Baumgarten's views. The primary effect of the bacillus of glanders on a tissue we found to be not a production of epithelioid cells, which undergo necrosis and invasion by leucocytes, as happens in the cases in which the bacillus of tuberculosis is concerned, but to be the production of primary necrosis of the tissue, followed by inflammatory exudation, often of a suppurative character. Degenerative changes rapidly ensue in the inflammatory products. These conclusions are in harmony with the observations of Tedeschi, above referred to.

The writer desires to acknowledge his obligations to Prof. W. T. Councilman and to Dr. F. B. Mallory for many valuable suggestions in the course of this work.

DESCRIPTION OF PLATES XIX AND XX.

Fig. 1.—Small glanders tubercle in the liver of a guinea-pig, dead twenty-one days after subcutaneous inoculation. High power. The chromatin bodies, leucocytes, etc., are shown. In the periphery are seen several of the deeply staining nuclei of liver cells. Stained with fuchsin and aurantia.

Fig. 2.—Two nodules in peritonæum of a guinea-pig, dead forty-eight hours after intraperitoneal inoculation. Low power. Stained with fuchsin and aurantia.

Fig. 3.—Showing composition of the material making up a large nodule in the tunica vaginalis of the testicle of a guinea-pig, dead forty-eight hours after inoculation into the peritoneal cavity. High power. The chromatin bodies and what were considered to be skeletons of dead cells and nuclei are shown. Stained with fuchsin and aurantia.

Fig. 4.—Tubule in cortex of kidney of guinea-pig, killed sixteen days after subcutaneous inoculation. High power. Showing the peculiar structures in the lumen and the appearance of the nuclei of the renal epithelium. Stained with fuchsin and aurantia.

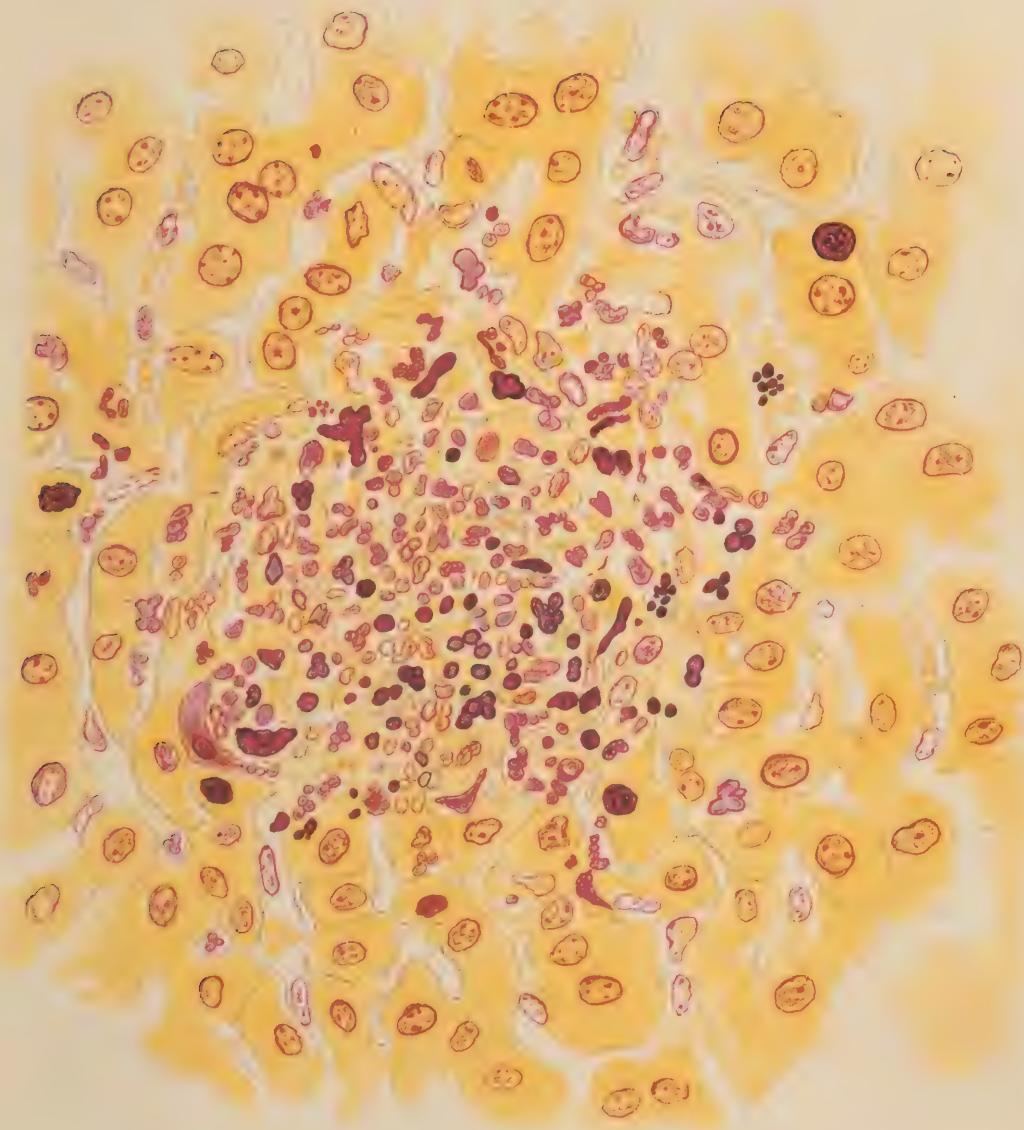


FIG. 1.

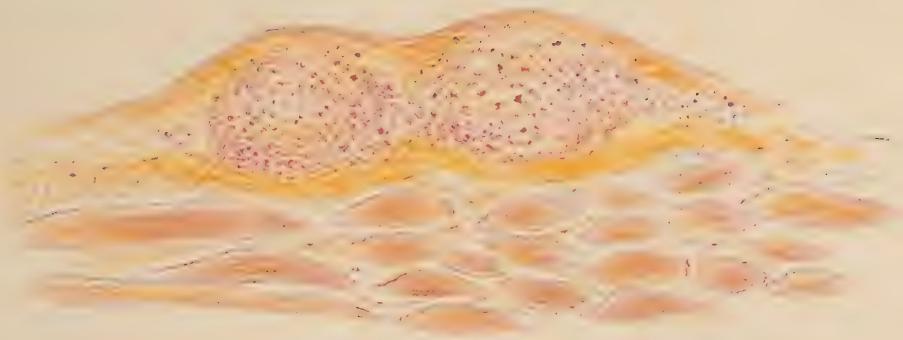


FIG. 2.



FIG. 3.

